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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,748	06/11/2001	John W. Sutherland	CDS-232	5214

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EXAMINER	
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ART UNIT	PAPER NUMBER
1637	12

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,748	SUTHERLAND, JOHN W.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-12 in Paper No.11 is acknowledged. The traversal is on the ground(s) that Group I is drawn to a method for detecting a mutation and Group II is drawn to a method for quantitating a nucleic acid having deletions. Applicant contends that the different inventions are not unrelated because one cannot quantitate a nucleic acid with a deletion without detecting it. Applicant states that indeed, quantitation, in this context, is detection with numerical specificity and deletions are mutations. Applicant contends that accordingly, it cannot be fairly said that Group I and Group II claims are drawn to unrelated processes such that restriction is required. Applicant further states that with respect to the sequences recited in Group III, the examiner is respectfully reminded that it is the position of the PTO that "to further aid the biotechnology industry in protecting its intellectual property without creating undue burden on the office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.1.41 *et. Seq.*, and permit a reasonable number of such nucleotide sequences in a single application," MPEP 803.04. Applicant contends that ordinarily, the PTO considers at least 10 sequences to be a reasonable number. In this case, the recited sequences are primers and probes (two primers and one probe per target). Thus the total of 22 claimed short sequences are well within the guidelines set by the Commissioner. Applicant concludes that in any cases, including all of the claimed inventions together does not pose a serious burden on the Examiner since searching with any of the fields of the various Groups of inventions will require a search of every field among the three Groups anyway.

This is not found persuasive because the searches of the different Groups are not coextensive because detection methods in the prior art are not necessarily combined with or is required for methods of quantitation or a composition of matter. It is further noted that the different inventions would require searching separate and non-overlapping areas which would constitute an undue search burden on the examiner because the composition of matter can function separately and distinctly from the different methods. Likewise, with respect to Applicant's arguments concerning a reasonable number of sequences to be search, it is noted that the MPEP 803.04 states that in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. The PTO office interprets "up to ten independent and distinct nucleotide sequences" as being equivalent to 1 or more sequence depending on the claims as written and specification. In this case, the composition of Group III only requires a single disclosed sequence. Likewise as noted in the prior Office action, the different sequences of Group III are structurally and chemically unrelated and requires undue search burden on the examiner if not restricted.

Upon further consideration of the claimed invention, Group II, claims 13-17, but not Group III will be combined with the elected Group I, claims 1-12 for prosecution on the merit. Non-elected claims 18-20 are withdrawn from consideration. Claims 1-17 are pending in the instant invention.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because of the following informalities:

(a) Table 1 beginning at pages 10-21 is unclear and confusing because it cannot be determined the actual purpose of the information recited therein or the information intended to be extrapolated therefrom. Clarification is required.

(b) At pages 24, 30, 34, 35, 40 and 42 the specification recites unit of measurements as "u", "ul", "u/ug", "U/ug". Appropriate correction is required.

(c) At pages 30, 33, 34 and 38, the specification contains brackets not intended to encompass an amendment (see 37 CFR 1.121 (e)(2)(ii)). It is suggested removing the brackets from the specification.

(d) At pages 31-39 and 41, the designation for the sequence identifier is improper (See MPEP 2422.03). It is suggested amending the disclosure by changing "Seq. ID. No." and "Seq. ID" to --SEQ ID NO:--.

Claim Objections

3. Claims 8, 12 and 15 are objected to because of the following informalities:

(a) The use of the trademark "TaqMan" has been noted in this application at claims 8 and 12. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

(b) Claim 15 is objected to for the abbreviation "wt" because abbreviations often have more than one meaning in the art. It is suggested reciting the full name of the abbreviation.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Todd et al (WO 96/32500, October 17, 1996). Regarding claim 1, Todd et al disclose a method of a detecting a nucleic acid comprising: (a) contacting a sample comprising nucleic acid with mutant PCR primers; (b) amplifying the product step (a) under short PCR conditions; and (c) identifying the presence of amplicons of step (b); wherein the presence of such amplicon is indicative of the presence of a nucleic acid sequence comprising a deletion, insertion or point mutation (see pages 4, line 15 to page 7, line 1; see also Examples).

Regarding claim 4, Todd et al teach the method of claim 1 further comprising the step of contacting the sample with a cleavage reagent (see pages 4, line 15 to page 7, line 1).

Therefore, Todd et al anticipates the limitations of claims 1 and 4.

5. Claims 1-3, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Herrnstadt et al (6,027,883, February 22, 2000). Regarding claims 1-3, 13, 15 and 16, Herrnstadt et al teach a method of detecting mutant nucleic acid comprising contacting a sample comprising mitochondrial DNA with mutant PCR primers; amplifying the product of step (a) under short PCR conditions and identifying the presence of amplicons of step (b) and further quantitating the presence of the amplicons by comparison with a wild-type standard (col. 7, lines 15-22, col. 19,

lines 34-52 and col. 31, lines 42 to col. 34, line 47). Therefore, the reference of Herrnstadt et al anticipates the limitations of claims 1-3, 13, 15 and 16.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 5, 7, 9, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herrnstadt et al as previously applied above in view of Todd et al. as previously applied above. Regarding claims 5, 7, 9, 11 and 14, Herrnstadt et al teach a method of detecting mutant nucleic acid comprising contacting a sample comprising mitochondrial DNA with mutant PCR primers; amplifying the product of step (a) under short PCR conditions and identifying the presence of amplicons of step (b) and further quantitating the presence of the amplicons by comparison with a wild-type standard. Herrnstadt et al additionally teach wherein primers were designed, e.g., forward and reverse primers, to detect the mutant target sequences in the sample along with the addition of four different nucleoside triphosphates and a DNA polymerase under conditions such that the DNA is amplified and detecting the amplicons (see col. 31-33).

The reference of Herrnstadt et al. differs from the instant invention in that the Herrnstadt et al do not expressly teach wherein a cleavage reagent is contacted in the samples containing a mixture of mutant DNA and wild type DNA such that only the mutant DNA is amplified preceding the addition of each of four different nucleoside triphosphates and a DNA polymerase.

In a method similar to that of Herrnstadt et al for detecting a mutant nucleic acid sequence, Todd et al. discloses a method comprising the steps of: contacting a sample suspected of containing a mutation, wherein said mutation is an insertion, deletion or point mutation, with a cleavage agent, contacting the sample with mutant PCR primers; amplifying the product under short PCR conditions in the presence of four different nucleoside triphosphates and a DNA polymerase, such that only the mutant DNA is amplified and detecting the presence of the amplified DNA (see pages 4-6). Todd et al teaches that the use of a cleavage agent in the method is advantageous in the PCR method because it results in the exclusive amplification of a mutant sequence (page 6, lines 3-5).

Therefore, in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the PCR detection method of Herrnstadt et al to incorporate a cleavage reagent as disclosed by Todd et al. One of ordinary skill in the art would have been motivated to do so for the advantage of exclusively amplifying mutant target sequences as suggested by Todd et al.

8. Claim6, 8, 10, 12, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herrnstadt et al in view of Todd et al and further in view of Whitcome et al. (Clinical Chemistry, Vol. 44, No. 5, pages 918-923, 1998). Regarding claims 6, 8, 10, 12 and 17, Herrnstadt et al in view of Todd et al. teach a method for detecting and quantifying mutant nucleic acid using short PCR conditions. The method of Herrnstadt et al. in view of Todd et al. differs from the instant invention in that the references do not teach wherein the method further comprises the step of contacting the samples with probes wherein said probes are selected from TaqMan probes,

Molecular beacons, PNA probes, DNAzymes or combination thereof. Nor does the references teaches wherein the nucleic acid is quantitated by real-time monitoring.

In a general teaching, Whitcombe et al. teach the use of a fluorescent assay for PCR amplicons. Whitcombe et al teaches that the method utilizes a single TaqMAn probe for the detection of any one target DNA sequence or a single pair of probes for genotyping any bi-allelic polymorphism in a PCR reaction for the quantitation of amplicons. Whitcombe et al. Teach that the method is useful for the single tube genotype analysis of a variety of human DNA polymorphisms and mutations (Abstract). Therefore in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the PCR mutation detection method of Herrnstadt et al in view of Todd et al to encompass a TaqMan probe(s) followed by quantitating by real-time monitoring. One of ordinary skill in the art would have been motivated to do for the advantage taught by Whitcome that the method is useful for the single tube genotype analysis of a variety of human DNA polymorphisms and mutations.

Conclusion

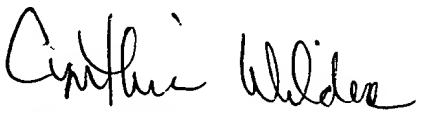
9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308 0196.

Cynthia B. Wilder, Ph.D.
Examiner
Art Unit 1637



CYNTHIA WILDER
PATENT EXAMINER

cbw
September 17, 2003